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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,396	08/30/2001	Kevin P. Baker	P2548P1C11	2338

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EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/944,396	Applicant(s) BAKER ET AL.	
	Examiner Elizabeth C. Kemmerer, Ph.D.	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The reply submitted 30 January 2003 (Paper No. 10), including the Goddard declaration submitted under 37 CFR 1.132, has been entered in full. Claims 1-21 are canceled. Claims 22-27 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

35 U.S.C. §§ 101 and 112, First Paragraph

Claims 22-27 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Claims 22-27 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The basis for these rejections is set forth at pp. 1-4 of the previous Office Action (Paper No. 8, 26 September 2002).

Applicant's arguments (pp. 2-4, Paper No. 10, 30 January 2003) have been fully considered but are not found to be persuasive for the following reasons.

Applicant refers to the attached Goddard declaration (filed under 37 CFR 1.132) as providing evidence that one skilled in the art accepts gene amplification data as an

indicator of cancerous tissue. The evidence presented in the declaration has been carefully considered. The examiner concedes that the declaration successfully addresses the concerns raised I the previous Office Action regarding the significance of a difference of 1 or 2 PCR cycles, and that proper controls for aneuploidy were used. Thus the nucleic acid molecule of SEQ ID NO: 68 would have utility, and would be enabled, as being useful as a probe to diagnose certain cancers.

However, the claims are directed to antibodies, not DNA. Applicant argues that antagonists such as antibodies directed against the proteins encoded by the DNAs would be expected to have utility in cancer therapy and as useful diagnostic agents. This arguments is not found to be persuasive, and the Goddard declaration under 37 CFR 1.132 filed 30 January 2003 is insufficient to overcome the rejection of claims 22-27 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth in the last Office action for the following reasons.

The data in the specification (and reviewed in the declaration) show that gene copy number is increased in certain tumor tissue samples. However, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that the antibodies would be useful diagnostically or as a target for cancer drug development. For example, Pennica et al. (1998, PNAS USA 95:14717-14722; Exhibit E of the declaration) disclose that,

> "An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in

the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left-hand column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors". Furthermore, an increase in mRNA expression does not necessarily result in increased protein expression. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript)p. 1863, second paragraph, and Figure 1).

Therefore, the claimed invention, directed to antibodies, remains rejected under 35 U.S.C. § 101 for lack of utility and 35 U.S.C. § 112, first paragraph, for lack of enablement.

35 U.S.C. § 112, Second Paragraph

Claims 22 and 27 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons set forth at p. 4 of the previous Office Action (Paper No. 8, 26 September 2002).

Applicant's arguments (pp. 4-5, Paper No. 10, 30 January 2003) have been fully considered but are not found to be persuasive for the following reasons.

Applicant provides definitions for "binds" and "specifically binds", and asserts that one skilled in the art recognizes these definitions. However, Applicant does not point to anywhere in the specification as supporting these definitions. Also, Applicant does not support that skilled artisans recognize these definitions by providing any evidence, such as references that provide such definitions. Therefore, Applicant's arguments are only assertions, unsupported by any evidence of record. Accordingly, the arguments are not found to be persuasive, and the rejection is maintained.

Priority Determination

As the claimed subject matter is found to lack utility and enablement under 35 U.S.C. §§ 101 and 112, first paragraph, respectively, the effective priority date for this application is the instant filing date, 30 August 2001. This determination was originally set forth at p. 5 of the previous Office Action (Paper No. 8, 26 September 2002).

Applicant argues (p. 6, Paper No. 10, 30 January 2003) that the utility and enablement issues have been overcome. This has been fully considered but is not found to be persuasive for the reasons set forth in the maintained rejection under 35 U.S.C. §§ 101 and 112, first paragraph, above.

Applicant also requests that a final determination of priority be delayed until after the utility rejection is finally resolved. Accordingly, the determination is maintained and

held in abeyance. Applicant need not address the issue again until after the utility issue has been resolved.

35 U.S.C. § 102

Claims 22-27 remain rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Holtzman et al. (US 6225085) as set forth at pp. 5-6 of the previous Office Action (Paper No. 8, 26 September 2002).

Applicant's arguments (pp. 6-8, Paper No. 10, 30 January 2003) have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that Holtzman does not disclose all of the limitations of the claims. Since the protein disclosed by Holtzman is only 98.4% identical to SEQ ID NO: 69 of the instant application, Applicant reasons that the antibody taught by Holtzman cannot be said to bind the polypeptide of SEQ ID NO: 69. Applicant argues that the differences between the two sequences are likely to confer different three-dimensional structure onto the polypeptides, thus affecting the ability of antibodies to bind the polypeptides. This has been fully considered but is not found to be persuasive. At 598 out of 673, the two proteins are absolutely identical. Holtzman discloses that polyclonal antibodies can be made. Since polyclonal antibodies are collections of antibodies that recognize different antigenic sites along a protein, it is reasonable to expect that a polyclonal antibody population would bind both proteins. Also, it appears that Applicant's arguments regarding the 102 rejection are in direct contradiction to their

arguments regarding the 112, second rejection, especially as regards antibodies that "bind" polypeptides.

Applicant also argues that the alignment (presented erroneously in Attachment A rather than B in the previous Office Action) fails to consider several differences between the polypeptides. Specifically, Applicant points to the 75 amino acids present in the prior art polypeptide and not present in the sequence recited in the claims. Due to this difference, the prior art polypeptide has 5 N-glycosylation sites whereas the recited polypeptide only has 3. Also, Applicant points to differences in the leucine-rich repeats between the two polypeptides. Applicant reasons that, due to these differences, the two polypeptides are likely to have vastly different three-dimensional structures. This has been fully considered but is not found to be persuasive. The sequences present in the prior art polypeptide but not present in the recited polypeptide do not correspond to major structural features such as signal sequence, transmembrane domain, EGF-like domain or fibronectin-like domain (see col. 54, lines 21-31 of Holtzman). Such domains have distinct three-dimensional structures and would be expected to present the same antigenic determinants. Furthermore, Applicant has not provided any evidence that the two polypeptides fold differently, such as a computer-generated folding image for the two sequences.

Therefore, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Mon. - Thurs., 6:30 to 4:00, and alternate Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elyabeth C. Kemmerer

ECK
March 6, 2003